<Division of Biochemistry> Chemical Biology

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- Chemical Biology -

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Visitors

Vis Prof QUIOCHO, Florante A	Baylor College of Medicine, U.S.A., 13 April–26 June 2009
Assoc Prof CHANG, Young-Tae	National Univeristy of Singapore, Singapore, 5 October 2009

Scope of Research

In human history, small organic molecules have been utilized for improving human health and for revealing secrets of life. Discovery or design of small organic molecules with unique biological activity permits small-molecule-initiated exploration of biology and further understanding of human diseases. Our laboratory has been discovering small organic molecules that modulate fundamental characteristics of human cells.

Research Activities (Year 2009)

Publications

Kamisuki S, Mao Q, Abu-Elheiga L, Gu Z, Kugimiya A, Kwon Y, Shinohara T, Kawazoe Y, Sato S, Asakura K, Choo H, Sakai J, Wakil SJ, Uesugi M: A Small Molecule that Blocks Fat Synthesis by Inhibiting the Activation of SREBP, *Chem. Biol*., **16 (8)**, 882-892 (2009).

Yamazoe S, Shimogawa H, Sato S, Esko J. D, Uesugi M: A Dumbbell-Shaped Small Molecule that Promotes Cell Adhesion and Growth, *Chem. Biol*., **16 (7)**, 773-782 (2009).

Jung D, Shimogawa H, Kwon Y, Mao Q, Sato S, Kamisuki S, Kigoshi H, Uesugi M: Wrenchnolol Derivative Optimized for Gene Activation in Cells, *J. Am. Chem. Soc*., **131 (13)**, 4774-4782 (2009).

Presentations

Small Molecules that Boost Cell Adhesion and Growth, Uesugi M, The 3rd Asia-Pacific International Peptide Symposium (APIPS), Jeju, Korea, 9 November 2009.

Small Molecule Tools for Cell Biology and Cell Therapy, Uesugi M, (Invited) CBI-KSBSB JOINT CONFERENCE, Busan, Korea, 6 November 2009.

Small Molecule Tools for Cell Biology, Uesugi M, (Invited) Combinatorial Chemistry and Chemical Biology toward A New Paradigm for Drug Discovery (CCCB), Osaka, 25 September 2009.

Small Molecules that Control Gene Expression, Uesugi M, 7th AFMC International Medicinal Chemistry Congress

Small-molecule Tools for Cell Biology and Cell Therapy

Knowledge about bioactive small molecules is a treasure of the humankind. Small organic compounds that the human being have discovered or synthesized from natural resources have been utilized for improving human health and for revealing secrets of life. The major goal of our research programs has been to expand the treasure by discovering and analyzing novel organic compounds with unique biological activities and to use them as tools to explore biology.

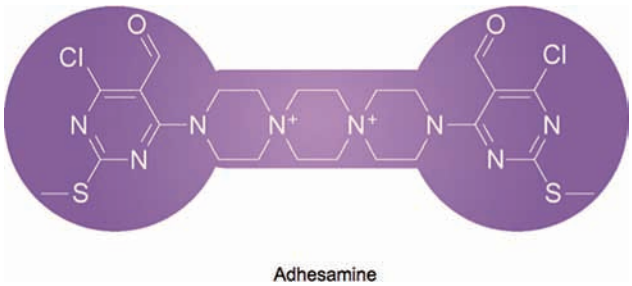
Our current research programs focus on discovering and using small organic molecules that modulate fundamental characteristics of human cells. In human history, bioactive small molecules have been utilized in three major applications: as medicines, as agrochemicals, and as molecular tools for basic biological research. Our laboratory is interested in exploring another application of small molecules: tools for cell therapy. Through screening chemical libraries, we have been discovering unique synthetic molecules that modulate or detect fundamental characteristics of human cells. Some of such molecules may serve as tools for cell engineering or cell therapy as well as basic cell biological research.

Adhesamine

One such example is the small molecule that we named "adhesamine". During an image-based phenotype screening of our chemical library, we noted a small molecule that boosts or enables the adhesion and growth of cultured human cells[1]. This unique molecule, adhesamine, promotes cell adhesion and growth of a range of cell types, including mouse iPS cells and primary cultured neurons. Chemical and cell biological experiments suggest that adhesamine targets selective cell-surface heparan sulfate for increasing cell adhesion and growth. Addition of adhesamine to the culture medium enables the adhesion of even floating lymphocytes to cell culture plates and the microinjection into them. Unlike poly-*L*-lysine, adhesamine induces apparently normal cell adhesion accompanied with organized actin structures and activation of focal adhesion kinase and ERK1/2 mitogen-activated protein kinases. In mouse hippocampal neurons, when compared with poly-L-lysine, adhesamine improves cell viability during long-term culture and enhances neuronal differentiation to matured neurons with less experimental periods[2].

Although the target of adhesamine is heparan sulfate (but not integrin), adhesamine often behaves like a small molecule version of fibronectin in cell culture and even in animals. Potential applications of adhesamine and its analogs will be discussed. Further synthetic and mechanistic studies of adhesamine may lead to the development of small molecule tools for cell biology and cell therapy.

(1) Yamazoe S, Shimogawa H, Sato S, Esko JD, Uesugi M: *Chem. Biol.*, 2009, **16**, 773-782 (2009).
(2) Hoshino M, Tsujimoto T, Yamazoe S, Uesugi M, Terada S: Submimitted.



Adhesamine

(AIMECS09), Cairns, Australia, 27 August 2009.

Synthetic Molecules that Control Gene Expression, Uesugi M, (Invited) 5th iCeMS International Symposium. Kyoto, 27 July 2009.

Grants

Uesugi M, Small-molecule Initiated Analysis of Cellular Signaling, Grant-in-Aid for Scientific Research (B), 1 April 2009–31 March 2012.

Uesugi M, Small Molecules that Promote the Production of iPS Cells, The Project for Realization of Regenerative Medicine, Japan Science and Technology Agency, 1 April 2008–31 March 2013.

Uesugi M, Practical Application of Small Molecules that Promotes Cell Adhesion, Adaptable and Seamless Technology Transfer Program through Target-Driven R&D, 1 November 2009–31 October 2010.

Kawazoe Y, Chemical Genetic Analysis of Vacuole Formation, Grant-in-Aid for Scientific Research (C), 1 April 2008–31 March 2011.

Awards

Yamazoe S, Poster Prize, Discovery and Mechanism of Adhesamine, A Dumbbell-shaped Small Molecule that Promotes Cell Adhesion, 4th Annual Meeting of Japanese Society for Chemical Biology, 19 May 2009.

Yamazoe S, Poster Prize, A Dumbbell-Shaped Small Molecule that Promotes Cell Adhesion and Growth, The 25th Naito Conference, 11 September 2009.